Amendments in the specification:

1) Please replace the paragraph beginning on line 17 of page 3 with the following paragraph:

US Patent No. 6,280,939 to Veeco Instruments, Inc. teaches a method and apparatus for DNA sequencing using a local sensitive force detector ~~DNA sequencing~~ that is performed in real time using an atomic force microscope (AFM). The AFM's probe detects motions that occur when a polymerase incorporates nucleotides into a growing polynucleotide chain and a newly formed double-stranded polynucleotide helix translocates (or "ratchets") through the polymerase's reaction site. These motions generate a mechanical force that is reflected, either directly or indirectly, by motion of the AFM cantilever. The resulting changes in cantilever motion are detected and can be recorded as an indication that a nucleotide has been incorporated into the DNA template. To determine which nucleotide type has been incorporated, a characteristic of the incorporation of at least one nucleotide type of interest is flagged so as to be distinguishable from the corresponding characteristics of the incorporation of nucleotides of other types.

2) Please replace the paragraph beginning on line 4 of page 4 with the following paragraph:

US Patent No. 6,238,871 to Sequenom, Inc. teaches a method to sequence DNA by mass spectrometry. The improvements of this method over the existing DNA sequencing technologies are high speed, high throughput, no electrophoresis and gel reading artifacts due to the complete absence of an

electrophoretic step, and no costly reagents involving various substitutions with stable isotopes. US Patent No. 6,238,871 utilizes the Sanger sequencing strategy and assembles the sequence information by analysis of the nested fragments obtained by base-specific chain termination via their different molecular masses using mass spectrometry, as for example, MALDI or ES mass spectrometry. A further ~~increase as~~ improvement US Patent No. 6,238,871 teaches is the throughput that can be obtained by introducing mass-modifications in the oligonucleotide primer, chain-terminating nucleoside triphosphates and/or in the chain-elongating nucleoside triphosphates, as well as using integrated tag sequences which allow multiplexing by hybridization of tag specific probes with mass differentiated molecular weights.

3) Please replace the paragraph beginning on line 10 of page 6 with the following paragraph:

In view of that which is stated above, it is ~~the~~ an objective of the present invention to provide an apparatus and method for DNA sequencing with a transcription protein and a nanoscale electrometer. ~~The~~ An advantage of the present invention over the prior art is that the system enables one to directly measure the DNA sequence as the transcription process unfolds.

4) Please replace the paragraph beginning on line 6 of page 8 with the following paragraph:

FIG. 2 shows an exemplary embodiment of DNA sequencing apparatus **200**. **FIG. 2** further shows an exemplary

embodiment of nanometer scale electrometer **110** that is used as one of the most sensitive devices and methods for measuring electronic charge. The device in this particular embodiment is called a single electron transistor **110A**. A reference to single electron transistor is, for instance, K.K. Likharev (1999), in a paper entitled "*Single-electron devices and their applications*," published in Proc. of the IEEE Vol. 87(4), page 606. The charge sensitivity of the single electron transistor is far superior to other prior art devices. It is four orders of magnitude more sensitive than electrometers based on the conventional field-effect transistor. For example, a single electron transistor has the capability of modulating a current flow of about 10^9 electrons per second by the presence of half an electron charge on the gate. However, the single electron transistor and field-effect transistor are similar in that they both control the current flowing between the source and drain by the electric field produced by an applied gate voltage. A single electron transistor contains a metal island **210** that is isolated from source **220** and drain **230** electrodes by thin tunnel junctions **240**. There are two effects that control the operation of a single electron transistor. First, the tunnel junctions **240** break the continuity of the classical electron flow into discrete electron units. Second, the Coulomb energy of metal island **210** regulates the number of electrons ~~electrodes~~ that can tunnel in and out of metal island **210**. Altering voltage **250** modifies the Coulomb energy, which controls the source-drain current. The single electron transistor will operate at room temperature if the length scale of tunnel junctions **240** is near 10 nm ~~μm~~. The tunnel junctions of the single

electron transistor of the present invention preferably ranges from ~~range of~~ 0.1 to 10 nm. The metal island of the single electron transistor of the present invention preferably ranges from 2 to 20 nm.

5) Please replace the paragraph beginning on line 14 of page 9 with the following paragraph:

Transcription protein **280** is first immobilized on gate **270** of single electron transistor **110A**. In a preferred embodiment, gate **270** is either constructed or coated with gold. The process of immobilizing a polymerase to a gold surface is well know to a person of ordinary skill in the art. For instance, Schafer et al. (1991, same reference as above) and Yin et al. (1995, same reference as above) have shown that RNA polymerase can be attached to a gold surface using a self assembling monolayer of ω-functionalized alkanethiols **285**. To sequence, transcription protein **280** is immobilized on gate **270** and an unknown strand of DNA **260** is delivered to the transcription protein **280**. During this process, the electronic charge configuration of the RNA and DNA together with the shape of the transcription protein will determine the electronic charge in the vicinity of single electron transistor **110A**. The electronic charge configuration corresponds to the nucleotide that is being replicated. Monitoring, with monitor **290** and leads **290A**, **290B**, the electronic charge configuration, or in other words, the source-drain conductance of single electron transistor **110A** as a function of time directly measures the dynamic electric field from the activities. DNA transcription occurs at a rate of 10-100 nucleotides per second. Typically a single

electron transistor has a charge sensitivity on the order of a hundredth of an electron with a 100 μs ~~ms~~ response time. Monitor **290** could be any type of monitoring device capable of detecting and monitoring the changes in nucleotides with the appropriate sensitivity. Monitor **290** is either an analog or an digital device. Monitoring device **290** could also include computing means in terms of software programs that run on a computer device to monitor, process and calculate any type of parameters from the obtained source-drain conductance. Each nucleotide has a distinct signature, and by correlating these signatures to the time domain output of the single electron transistor, the DNA is sequenced.

6) Please replace the paragraph beginning on line 13 of page 10 with the following paragraph:

FIG. 3 shows exemplary embodiment of DNA sequencing apparatus **300** according to the present invention. **FIG. 3** shows another exemplary embodiment of a nanometer scale electrometer **110** that could also be used in the present invention to measure electronic charge. The device in this particular embodiment is a nanoparticle device **110B**. The difference between nanoparticle device **110B** and single electron transistor **110A** is that in case of nanoparticle device **110B**, the charge generated by the transcription process passes through nanoparticle device **110B** and is detected by monitor **290**. In case of single electron transistor **110A** a voltage needs to be applied to generate Coulomb energy which controls the source-drain current. Single electron transistor **110A** is then able to sense the charge generated by the transcription process.

Nanoparticle device **110B** includes a nanoparticle **310** that is positioned in between two electrodes **320A** and **320B**. The immobilization of transcription protein **330** to nanoparticle **310** is done in a similar way as mentioned above in relation to **FIG. 2**. Nanoparticle **310** is preferably a gold nanoparticle and is less than 2 nm in diameter to work at room temperature. In order for nanoparticle **310** to directly observe the electronic charges, a sensitivity on the order of a hundredth of an electron with a 100 ~~ms~~ μs response time is preferred.

7) Please replace the paragraph beginning on line 5 of page 11 with the following paragraph:

The DNA sequencing devices shown in **FIGS. 2** and **3** could be constructed on an integrated circuit chip as shown by schematic circuit chips **400** and **500** shown in **FIG. 4** and **FIG. 5** respectively. Integrated circuit chips commonly span a square centimeter and a plurality of DNA sequencing devices of the present invention could be constructed on the chip. A single DNA sequencing device as shown in **FIG. 2** typically occupies a surface of 10 μm^2 ~~mm^2~~. With integrated circuit chips commonly spanning a square centimeter, it is feasible that a million DNA sequencing devices as shown in **FIG. 2** could be constructed in parallel. If a million DNA sequencing devices in parallel sequenced at a rate of 100 nucleotides per second, the entire human genome of 3 billion base pairs could be sequenced in less than a minute.